Remarks

Claims 1-30 were pending. Due to the restriction requirement, claims 25-30 are withdrawn without prejudice. No claims are added. Therefore, claims 1-24 are now pending.

Claim 1 was amended to clarify that it is the mRNA of the complexes of mRNA, ribosome and displayed specific binding member that is encapisdated. Support for this amendment can be found throughout the application, for example in Example 4 starting on page 31, line 25.

Species Election Requirement

Applicants hereby reserve the right to Petition the Commissioner for Requirement for Restriction. In addition, Applicants request that when the generic claim is found to be allowable, additional species be rejoined by the Examiner. As discussed below, the claimed species, and claim 1, are patentable over the cited documents.

Specification

The specification has been amended to include the priority information, as suggested by the Examiner.

35 U.S.C. § 103(a)

Claims 1, 8-14 and 21-23 were rejected as unpatentable over Plunkthun et al. (WO 98/48008), Dubois et al. (WO 98/00547) and Landt et al. (Gene 96:125-8, 1990). Applicants respectfully disagree and request reconsideration.

It appears that this rejection is based generally on the combination of a document teaching ribosome display (Plunkthun *et al.*) and a document that teaches encapisdation of RNA (Dubois *et al.*). However, the encapisdation in a viral coat of mRNA of a complex of mRNA, ribosome and displayed specific binding member in a method as claimed in claim 1 is non-obvious.

The teaching of Dubois *et al.*, when read properly in context, emphasizes the non-obviousness of the present claims, since its teaching is contrary to the achievement and practice

of the present claims. In particular, Dubois *et al.* teaches that encapsidation in the bacteriophage proteins prevents translation of the RNA (see for example the passage bridging pages 11 and 12), and moreover, that prior to translation for "transient gene expression in vitro and in vivo" (as referred to on page 14 of the Office Action) it is required to extract the RNA from the particles. Fro example, Dubois *et al.* states in the paragraph bridging pages 10 and 11:

> "In a specific preferred embodiment, the invention relates to a ribonuclease resistant recombinant RNA ("reRNA") standard. These Armored RNA™ (AR) standards are riobonuclease resistant due to the encapsidation of the reRNA by baceteriophage proteins. The intact RNA is easily extracted from the Armored RNA™ standard particles by common RNA extraction methods such as the guanidinium and phenol method (Chomczynski, 1987). The non-bacteriophage RNA may be used in many applications: as an RNA standard for quantification, as RNA size standards, and for transient gene expression in vitro and in vivo."

The Office Action refers only to the last sentence, but overlooks the explicit teaching that the "non-bacteriophage RNA" that is the subject of that sentence is "extracted from the Armored RNA™ standard particles by common RNA extraction methods". It is non-bacteriophage RNA that is to be translated subsequent to such extraction.

The present claims are based in part on the findings reported in the application (see for example, Example 4) that mRNA of an mRNA, ribosome and displayed protein complex can be packaged. As discussed on page 8 of the application, it was not obvious that this could be achieved. In addition, documents cited in the application, including Hwang *et al.* (*Proc, Natl. Acad. Sci. USA* 91:9067-71, 1994; see pages 17 and 35 of the application), support the non-obviousness. In summary, there was no basis in the art for any reasonable expectation of success.

Even if one skilled in the art would combine Pluckthun *et al.* and Dubois *et al.*, it is clear that Dubois *et al.* teaches a requirement to dissociate RNA from viral coat before translating, consistent with the teaching of others of steric exclusion of ribosome binding and virus assembly (for example see Hwang *et al.*, *Proc, Natl. Acad. Sci. USA* 91:9067-71, 1994). In contrast, the claims of the present application include mRNA of complexes of mRNA, ribosome and displayed protein that is encapsidated.

Claims 9 and 21 were rejected as unpatentable over Plunkthun *et al.* (WO 98/48008) and Landt *et al.* (*Gene* 96:125-8, 1990). Applicants respectfully disagree and request reconsideration. Landt *et al.* does not disclose either ribosome display or RNA encapsidation. Therefore, one of skill in the art would not be motivated to combine the teaching of Landt *et al.* with Plunkthun *et al.*.

Therefore, the present claims are nonobviousness over the prior art, and Applicants request that the 35 U.S.C. § 103(a) rejection be withdrawn. If any issues remain before a Notice of Allowance is issued, the Examiner is invited to telephone the undersigned.

Respectfully submitted,

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